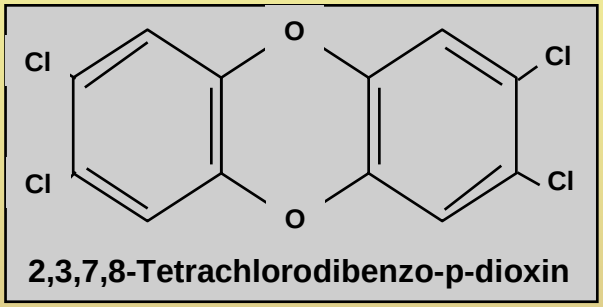
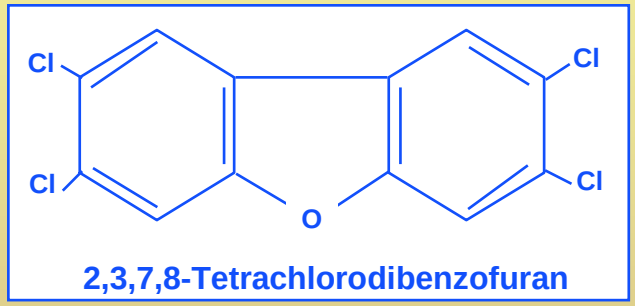
Dioxin and Dioxin-Like Compounds: Science Overview

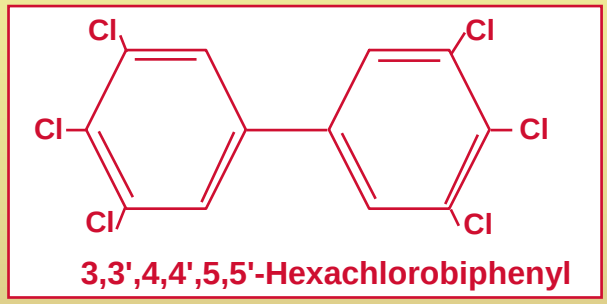
Dioxin-Like Compounds



2,3,7,8-Tetrachlorodibenzo-p-dioxin



2,3,7,8-Tetrachlorodibenzofuran



3,3',4,4',5,5'-Hexachlorobiphenyl

Dioxins
75 congeners
7 toxic

2,3,7,8-TCDD
1,2,3,7,8-PeCDD
1,2,3,4,7,8-HxCDD
1,2,3,6,7,8-HxCDD
1,2,3,7,8,9-HxCDD
1,2,3,4,6,7,8-HpCDD
1,2,3,4,6,7,8,9-OCDD

Furans
135 congeners
10 toxic

2,3,7,8-TCDF
1,2,3,7,8-PeCDF
2,3,4,7,8-PeCDF
1,2,3,4,7,8-HxCDF
1,2,3,6,7,8-HxCDF
1,2,3,7,8,9-HxCDF
2,3,4,6,7,8-HxCDF
1,2,3,4,6,7,8-HpCDF
1,2,3,4,7,8,9-HpCDF
1,2,3,4,6,7,8,9-OCDF

PCBs
209 congeners
12 toxic

3,3',4,4'-TeCB
3,3',4,4',5-PeCB
3,3',4,4',5,5'-HxCB
Plus 8 others

Toxic Equivalency (TEQ)

Reassessment Chapter Summarizes Scientific Support

- *Based on inspection of multiple endpoints and/or receptor binding (WHO criteria)*
- *Fundamental to evaluation of this group of compounds*
- *Having growing empirical basis and being theoretically sound*
- *WHO_{98} internationally accepted*

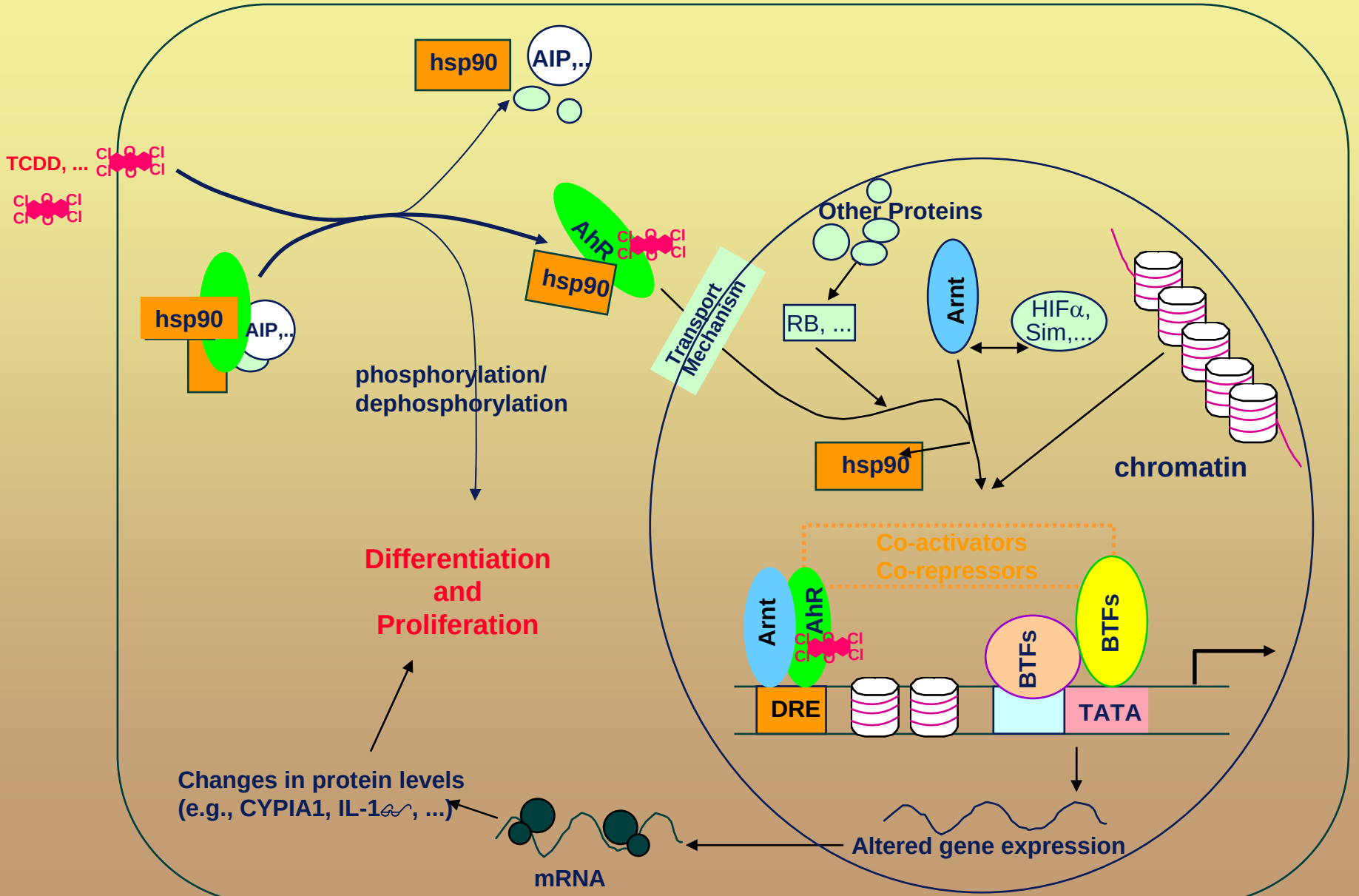
Five Compounds Make up About 80% of the Total TEQ in Human Tissue

Four of 17 Toxic CDD/CDF Congeners

One of the 12 toxic PCBs

- ***2,3,7,8-TCDD***
- ***1,2,3,7,8-PCDD***
- ***1,2,3,6,7,8-HxCDD***
- ***2,3,4,7,8-PCDF***
- ***PCB 126***

Modes of Action of Dioxin



Body Burden Best Dose Metric (Ng/Kg BW)

- *Accounts for differences in half-life*
- *Results in strong agreement between human and animal data*
- *Adopted by WHO, EC, HHS*

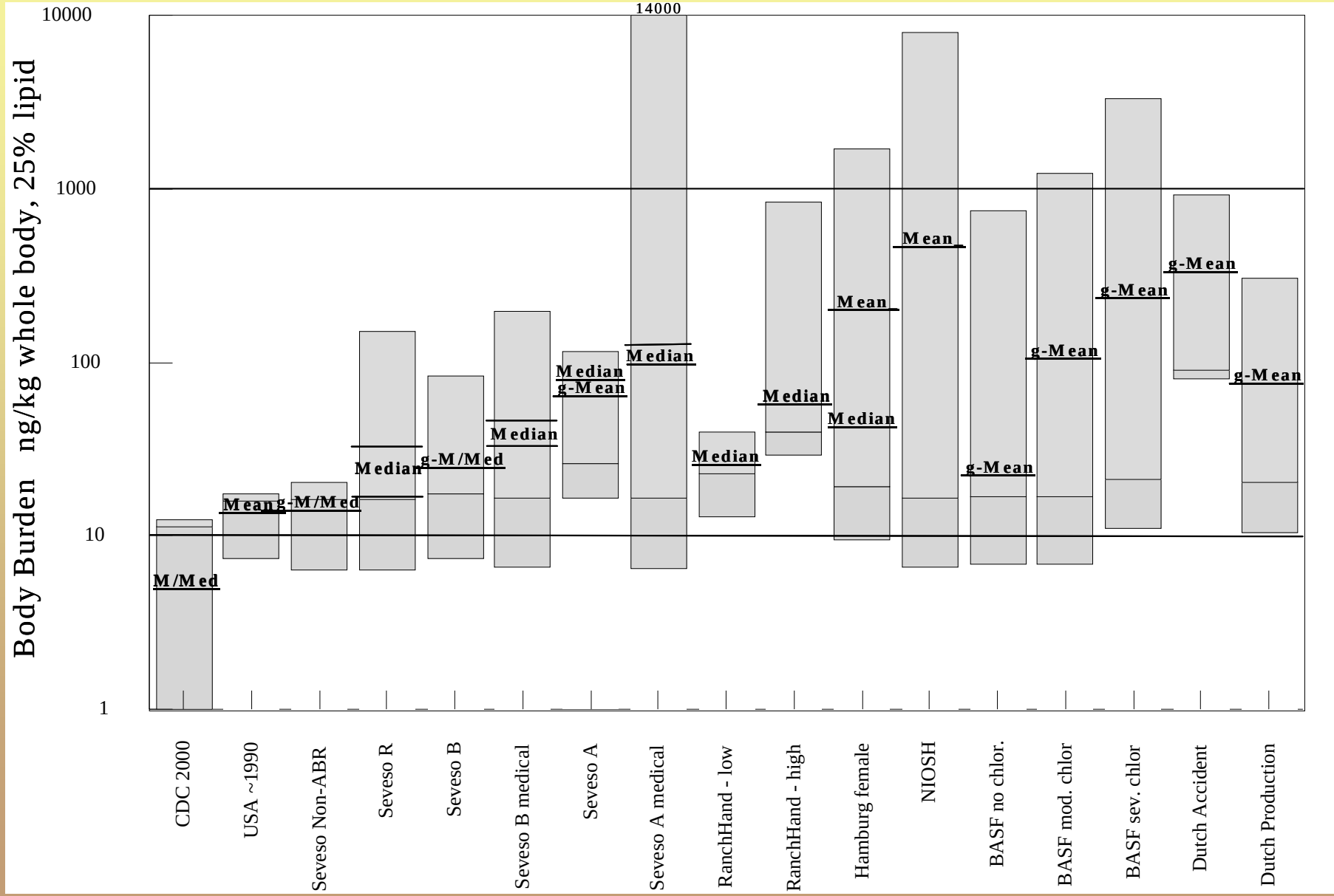
Summary of All Site Cancer ED_{01}s and Slope Factor Calculations

STUDY	ED_{01} (95% lower bound) ng/kg	Slope factor, All cancer risk/pg/kg/day
Hamburg cohort, Becher et al. 1998	2.1 – 16.8	$1.8 – 14 \times 10^{-3}$
NIOSH cohort, Steenland et al. 2001	2.9 – 21	$1.4 – 10 \times 10^{-3}$
BASF cohort, Ott and Zober, 1996*	80.2 (37.5)	(0.80×10^{-3})
Sprague-Dawley rats, Kociba et al. 1978; Goodman and Sutter, 1992 (pathology)	31.9 (22) BMD dose 38 (27.5) BMD dose	(1.4×10^{-3}) (1.1×10^{-3})

Upper bound estimates in parentheses

*Calculated by NIEHS/Chapter 8 (EPA, 2000)

Peak Dioxin Body Burden Levels in Background Populations and Epidemiological Cohorts (Back-calculated)



Dioxins and Human Carcinogenicity

2,3,7,8-TCDD	➔	**Carcinogenic to humans**
Other dioxin-like compounds	➔	**Likely to be carcinogenic**
Complex Environmental Mixtures	➔	**Likely to be carcinogenic**

Based on:

- **Unequivocal animal carcinogen**
- **Limited human information (epidemiological/other)**
- **Mechanistic plausibility**

Cancer potency increasingly focusing on human studies

Note: (IARC) classified TCDD as a Category 1, “Known” human carcinogen. DHHS 9th Report on Carcinogens (ROC) the same

Quantitative estimate of cancer risk

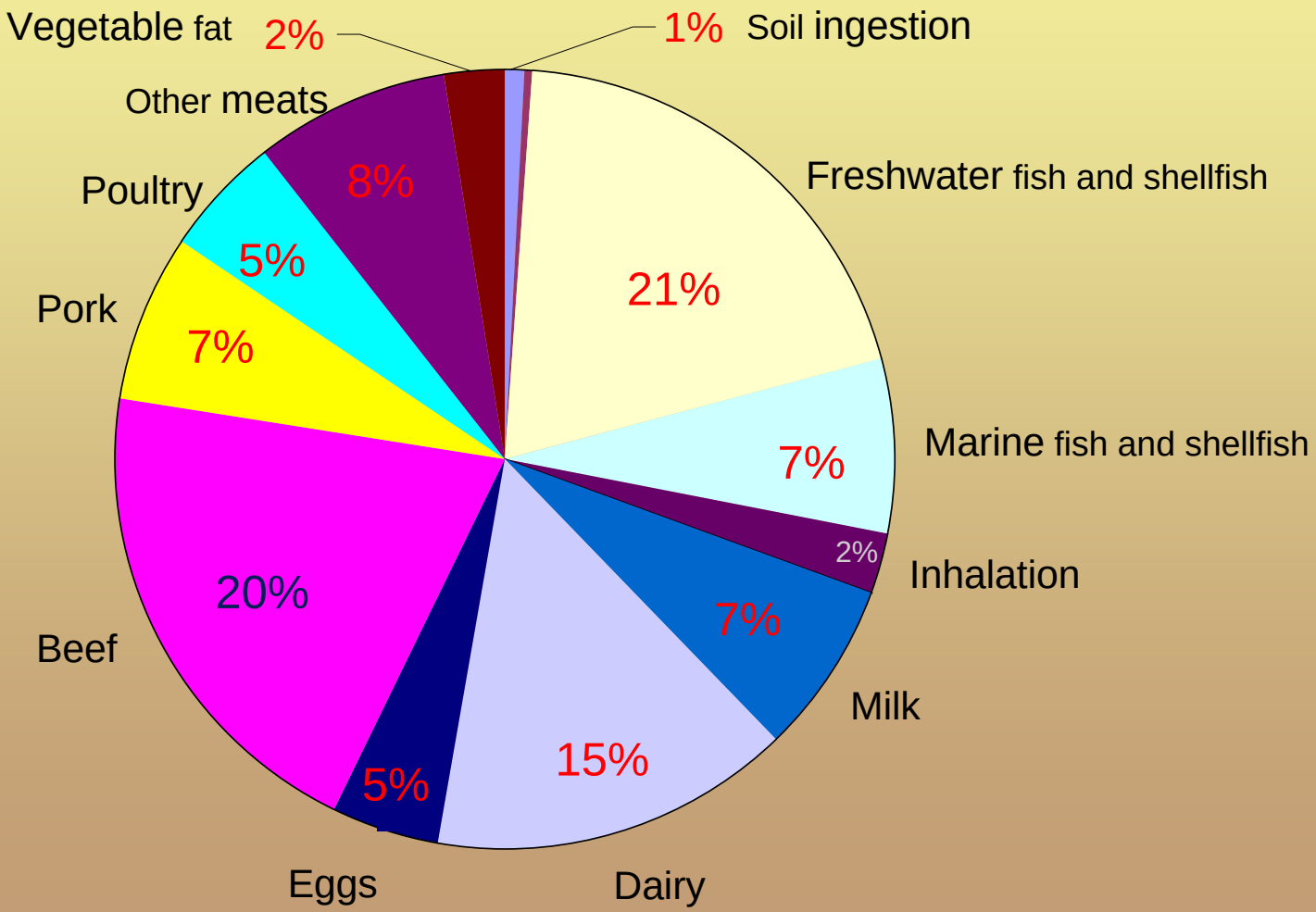
- **Cancer slope factor is revised upward by a factor of ~6 over the 1985 EPA value**
- **Cancer risks to the general population may exceed 10^{-3} (1 in 1,000) from background (dietary) exposure but are likely to be less and may even be zero for some individuals**

Body Burdens Associated With Non-Cancer Effects

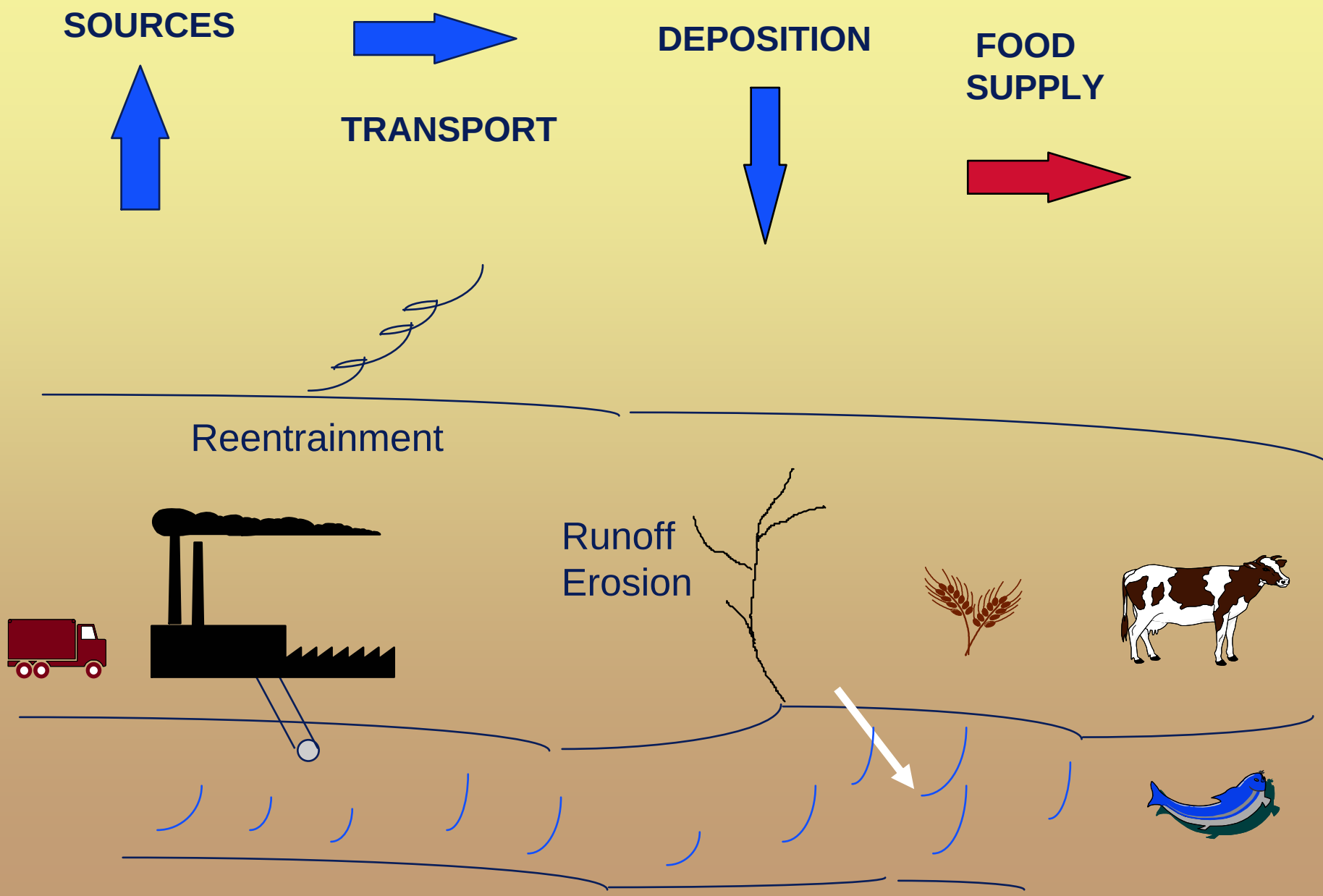
Adverse Effects	**Ng/Kg**	**MOE***
➢ *Developmental neurotoxicity:*	22	4
➢ *Developmental/reproductive toxicity:*	0.7 - 42	0.1 - 8
➢ *Developmental immunotoxicity:*	50	10
➢ *Adult immunotoxicity:*	1.6 - 12	0.3 - 2
➢ *Endometriosis:*	22	4
Biochemical Effects		0.6 - 16
➢ *CYP1A1 Induction:*	0.6 - 33	0.1 - 7
➢ *CYP1A2 Induction:*	2.1 - 83	0.4 - 17

***MOE = effect level / current average U.S. background body burdens of 5 Ng/Kg**

Relative Contribution of Different Exposure Routes to Typical General Population Exposure



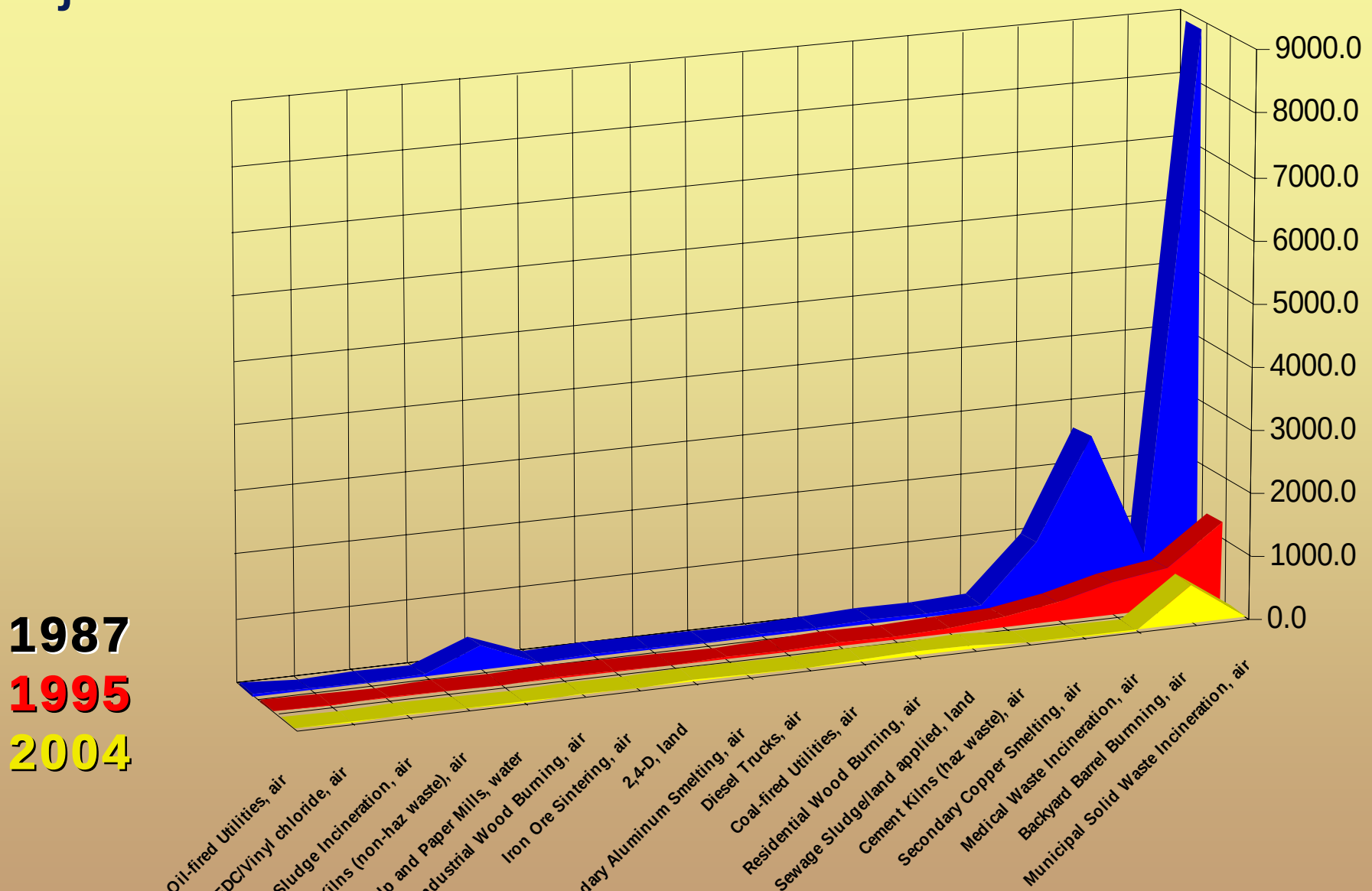
Sources and Pathways to Human Exposures



Inventory of Sources of Dioxin in the United States-May, 2000	*1987 Emissions (g TEQdf-WHO98/yr)*	*1995 Emissions (g TEQdf-WHO98/yr)*	*2002/4 Emissions (g TEQdf-WHO98/yr)*
Municipal Solid Waste Incineration, air	8877.0	1250.0	*12.0*
Backyard Barrel Burning, air	604.0	628.0	*628.0*
Medical Waste Incineration, air	2590.0	488.0	*7.0*
Secondary Copper Smelting, air	983.0	271.0	*5.0*
Cement Kilns (haz waste), air	117.8	156.1	*7.7*
Sewage Sludge/land applied, land	76.6	76.6	*76.6*
Residential Wood Burning, air	89.6	62.8	*62.8*
Coal-fired Utilities, air	50.8	60.1	*60.1*
Diesel Trucks, air	27.8	35.5	*35.5*
Secondary Aluminum Smelting, air	16.3	29.1	*29.1*
2,4-D, land	33.4	28.9	*28.9*
Iron Ore Sintering, air	32.7	28.0	*28.0*
Industrial Wood Burning, air	26.4	27.6	*27.6*
Bleached Pulp and Paper Mills, water	356.0	19.5	*12.0*
Cement Kilns (non-haz waste), air	13.7	17.8	*17.8*
Sewage Sludge Incineration, air	6.1	14.8	*14.8*
EDC/Vinyl chloride, air	NA	11.2	*11.2*
Oil-fired Utilities, air	17.8	10.7	*10.7*
Crematoria, air	5.5	9.1	*9.1*
Unleaded Gasoline, air	3.6	5.9	*5.9*
Hazardous Waste Incineration, air	5.0	5.8	*3.5*
Lightweight ag kilns, haz waste,air	2.4	3.3	*0.4*
Kraft Black Liquor Boilers, air	2.0	2.3	*2.3*
Petrol Refine Catalyst Reg., air	2.2	2.2	*2.2*
Leaded Gasoline, air	37.5	2.0	*2.0*
Secondary Lead Smelting, air	1.2	1.7	*1.7*
Paper Mill Sludge, land	14.1	1.4	*1.4*
Cigarette Smoke, air	1.0	0.8	*0.8*
EDC/Vinyl chloride, land	NA	0.7	*0.7*
EDC/Vinyl chloride, water	NA	0.4	*0.4*
Boilers/industrial furnaces, air	0.8	0.4	*0.4*
Tire Combustion , air	0.1	0.1	*0.1*
Drum Reclamation, air	0.1	0.1	*0.1*
TOTALS	13,995	3,252	*1,106*
Percent Reduction from 1987		77%	92%

***** It is important to note that the source inventory of the reassessment only addressed 1987 and 1995. The 2002/4 values projected in this table are only preliminary and are based primary on emission reduction projections developed as a part of EPA rule makings. The 2004 numbers have not had the benefit of independent peer review and public comment as has the reassessment inventory. EPA is currently in the process of developing a detailed inventory for the year 2000.

Major US Dioxin Sources



Poorly Characterized Sources

Secondary steel electric arc furnaces

Coke production

Ceramic manufacturing

Clay processing

Ferrous and non-ferrous foundries

Asphalt mixing plants

Primary magnesium

TiO_2

Wood stoves

Forest fires

Brush fires

Range fires

Ag burning

Landfill fires

Structural fires

Landfill flares

Rural soil erosion to water

Urban runoff to surface water

Utility poles and storage yards

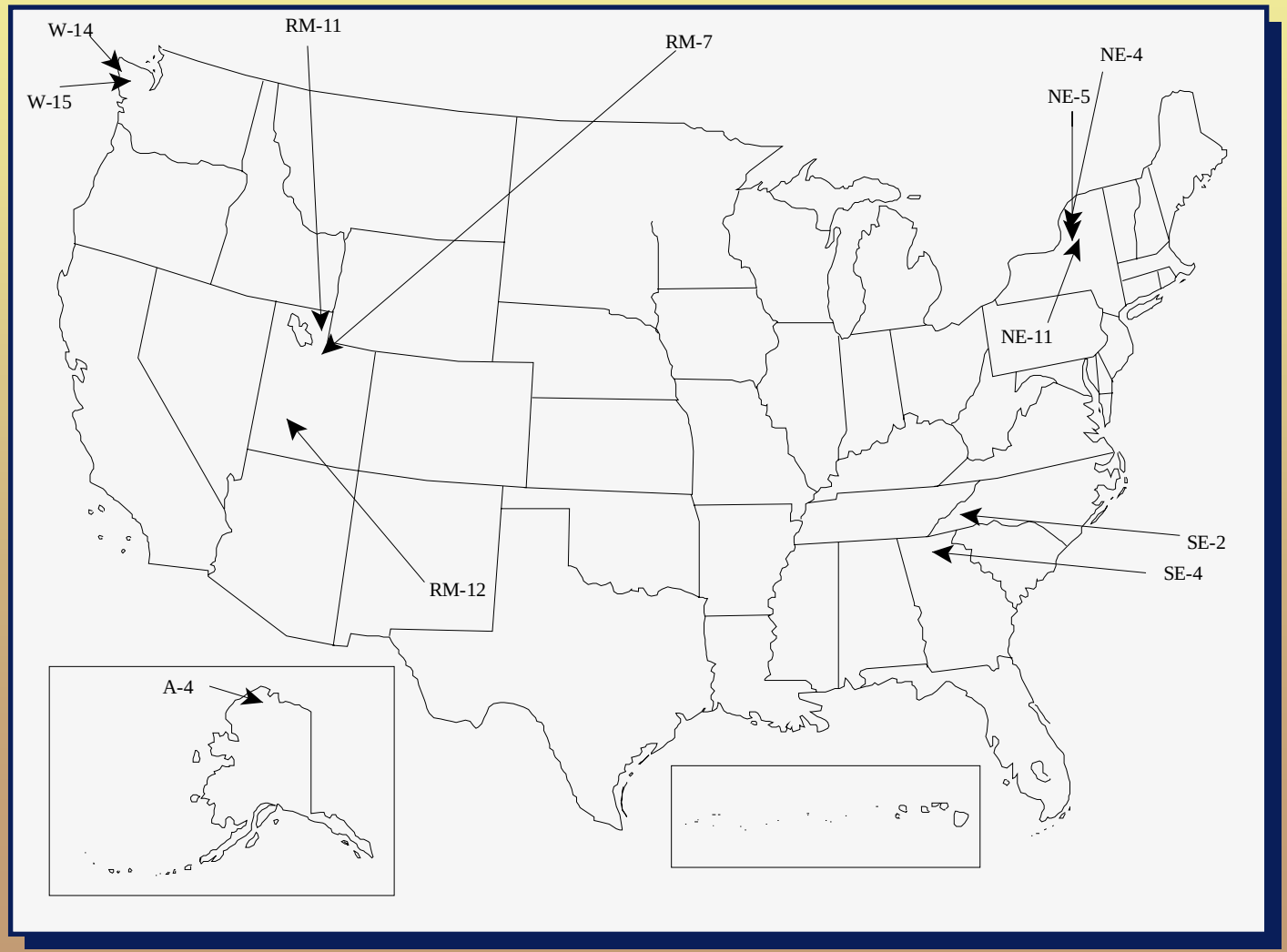
Landfill fugitive emissions

Transformer storage yards

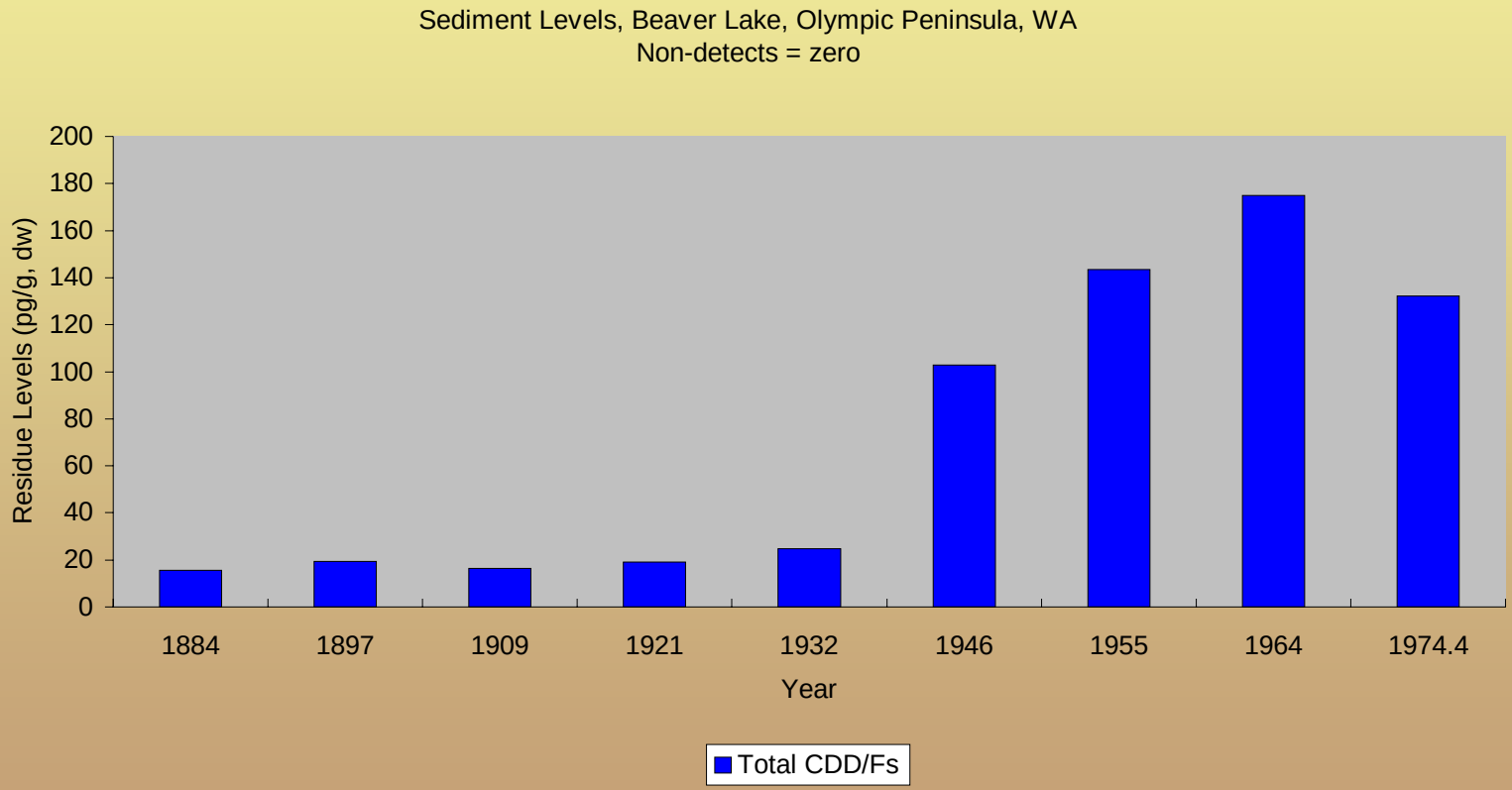
Reservoir Sources

- **Old releases of dioxins that are temporarily stored in environmental compartments to later be reintroduced into the circulating environment**
- **Contribute as much as 50% of general population**
- **Dioxin-like PCBs more than a third of total risk**

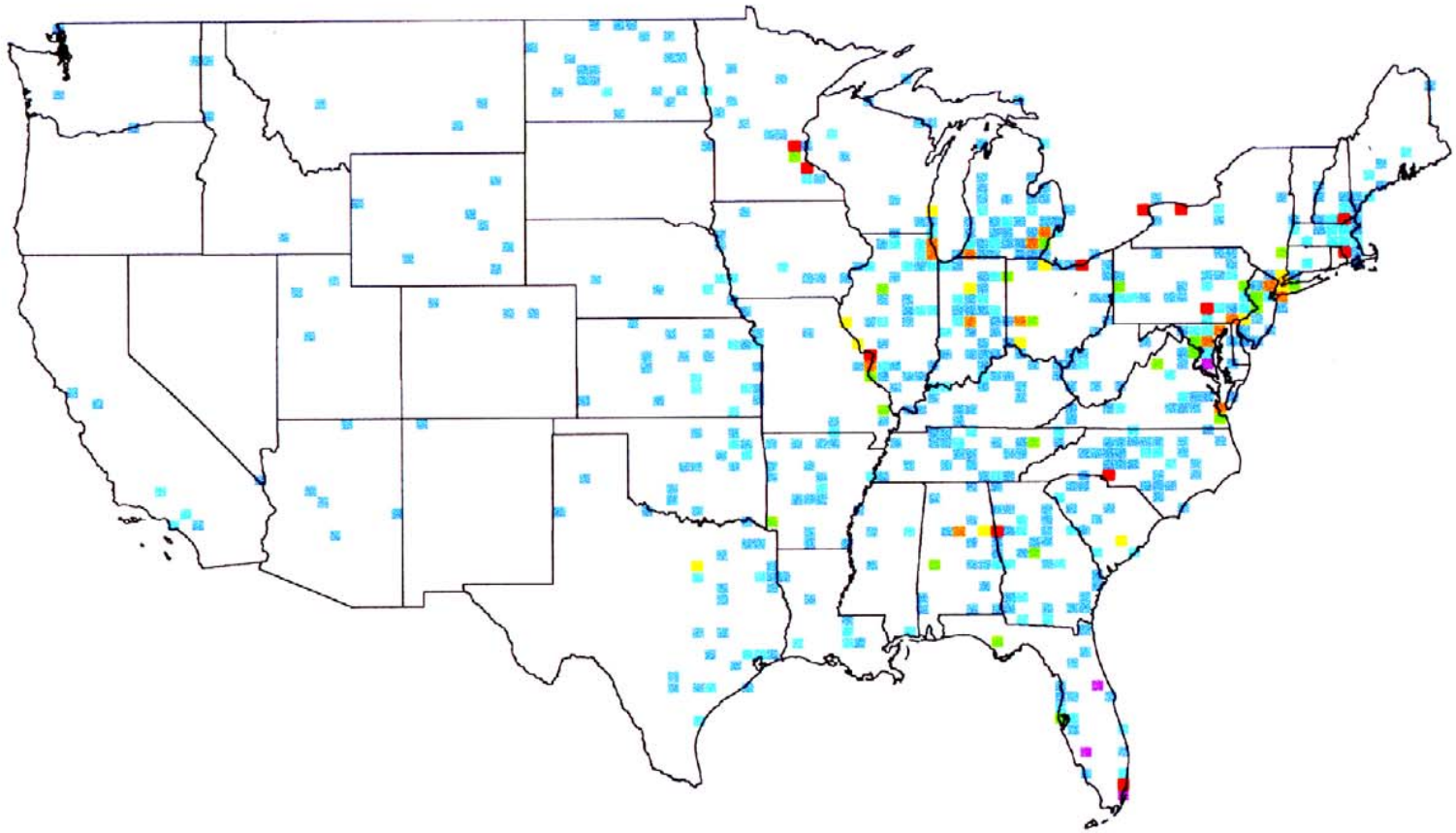
Location of Lakes for Sediment Core Sampling



20th Century Trend



Top 80-percent Emitting Sources, Dioxin/Furan TEQ Emissions



Units of µg/hr; number of cells in each range in ( )

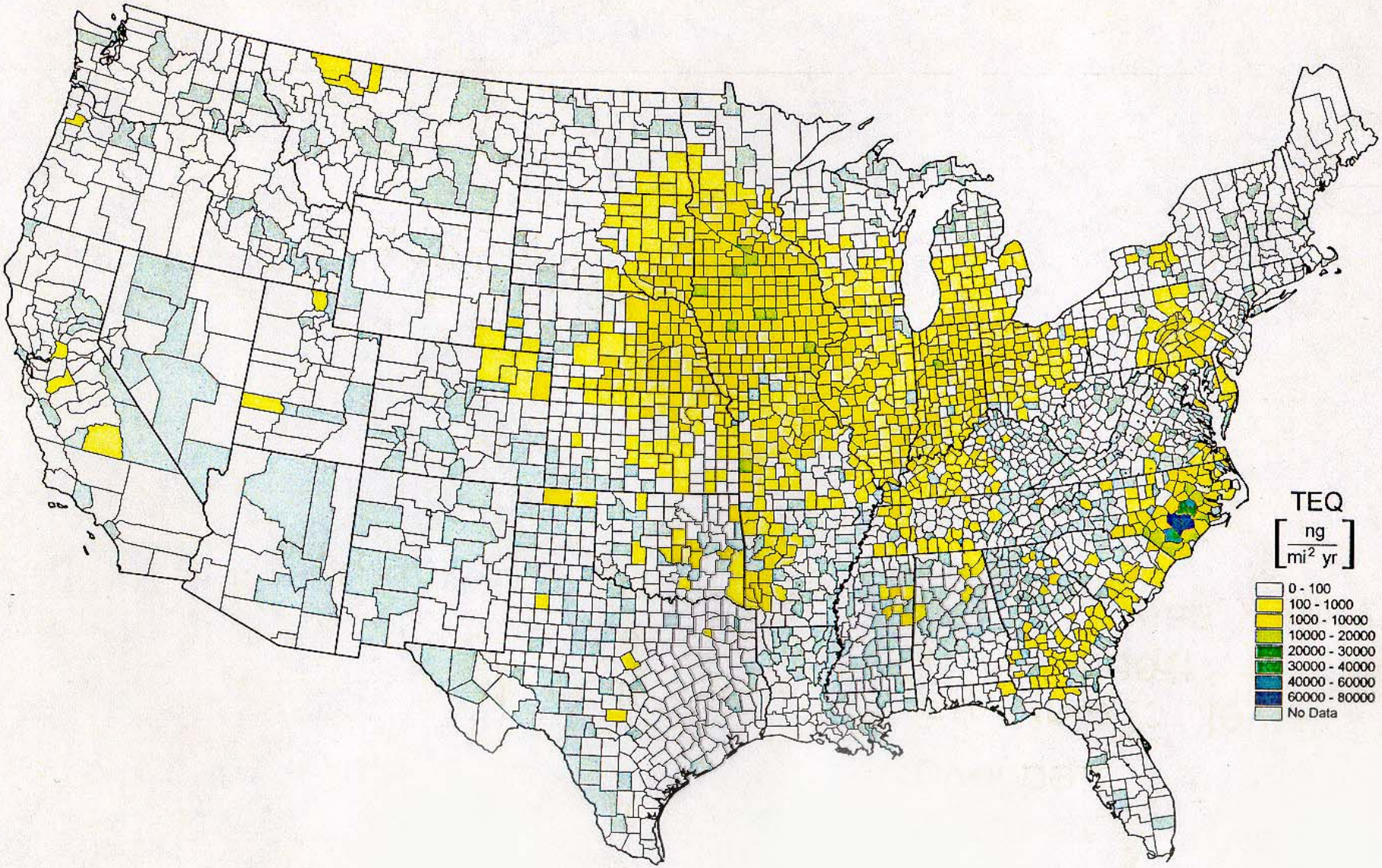
- 1-10 (4)
- 10 - 100 (391)
- 100 - 500 (115)
- 500 -1000 (23)
- 1000 - 2000 (12)
- 2000 - 5000 (15)
- 5000 - 22377 (12)

N

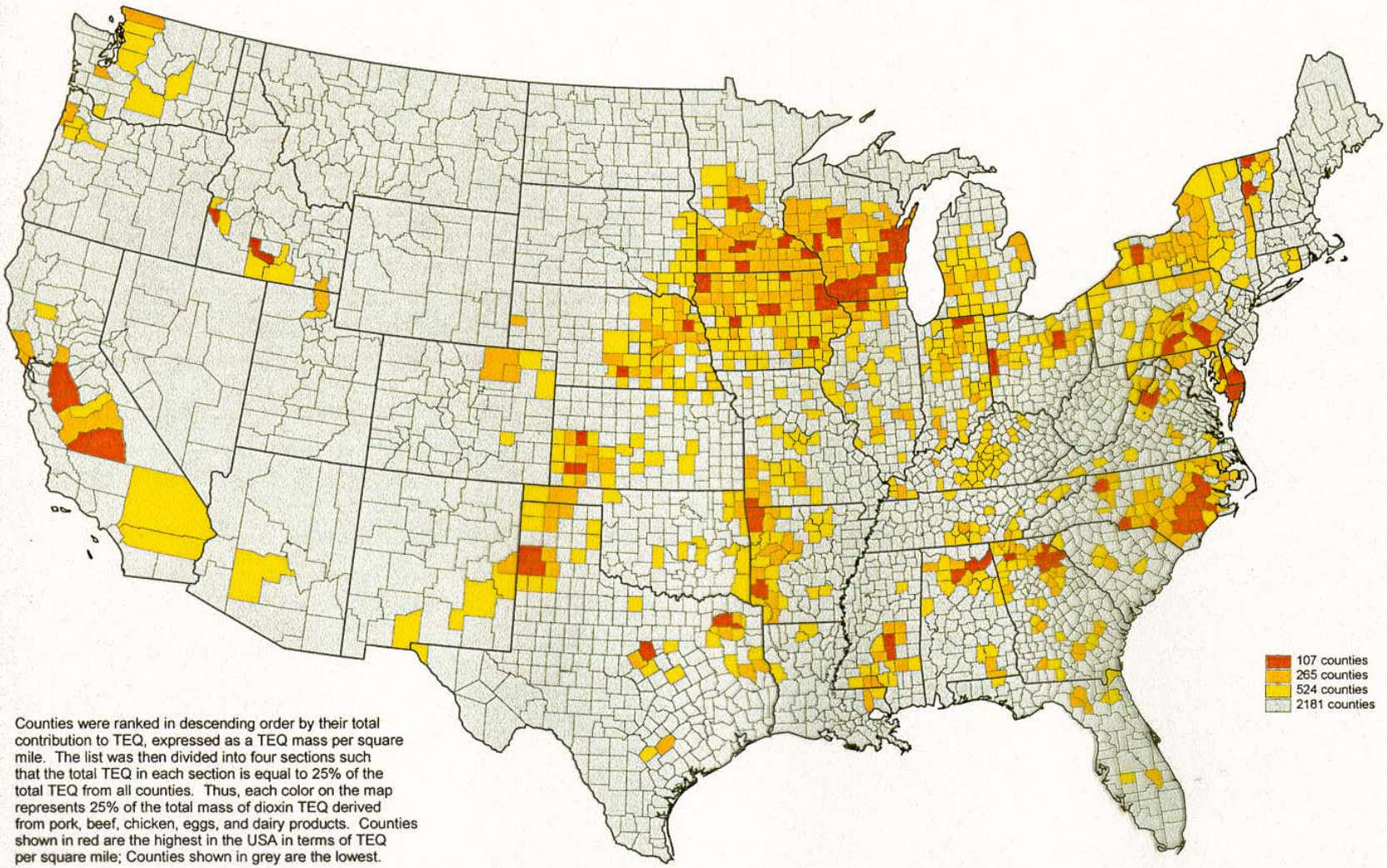
KM

0 500 1000

TEQ Derived from Pork

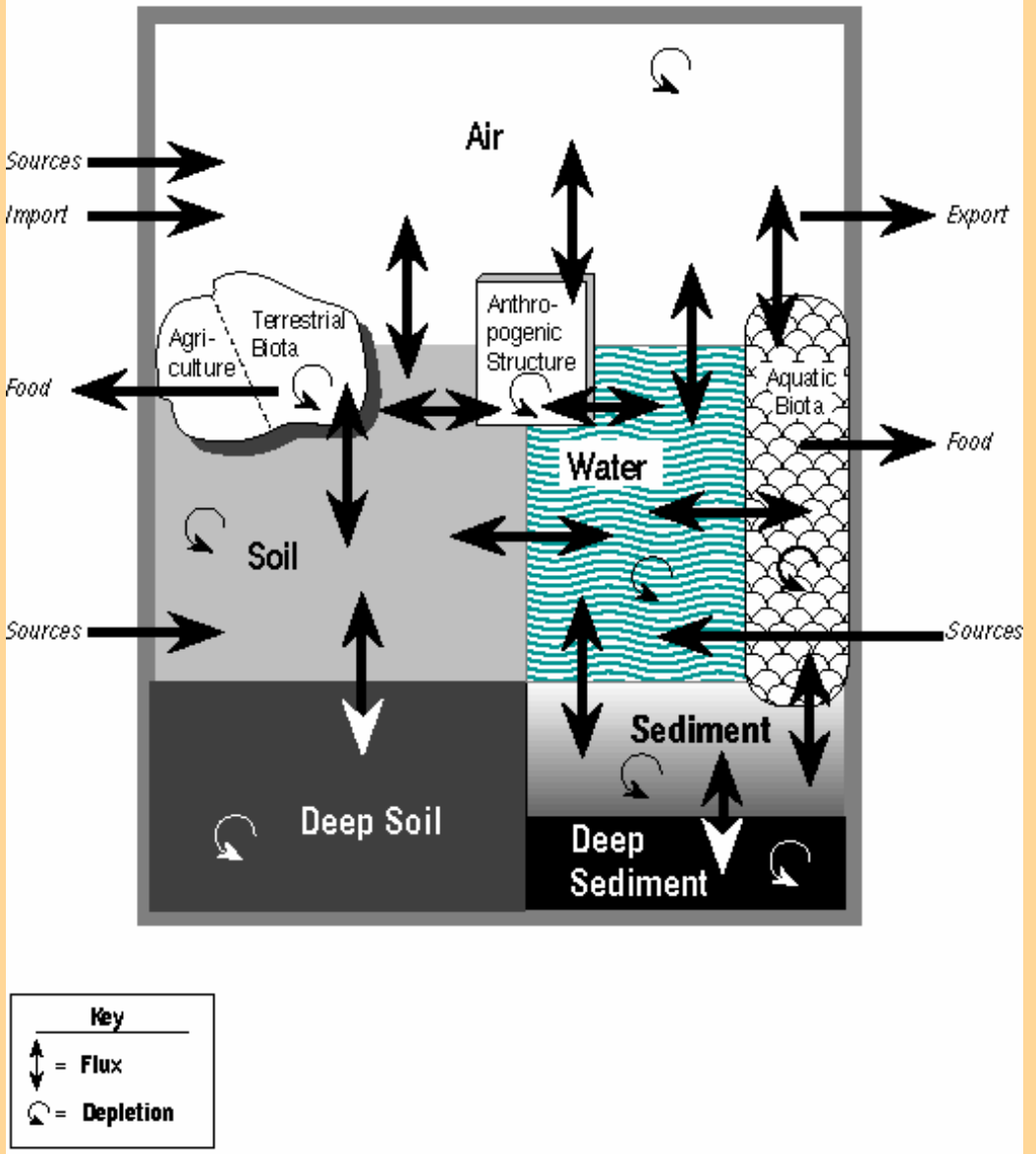


Dioxin Uptake Into Meat And Dairy



Counties were ranked in descending order by their total contribution to TEQ, expressed as a TEQ mass per square mile. The list was then divided into four sections such that the total TEQ in each section is equal to 25% of the total TEQ from all counties. Thus, each color on the map represents 25% of the total mass of dioxin TEQ derived from pork, beef, chicken, eggs, and dairy products. Counties shown in red are the highest in the USA in terms of TEQ per square mile; Counties shown in grey are the lowest.

Fluxes among dioxin reservoirs



Fluxes Among Dioxin Reservoirs

Background Serum Levels in the United States 1995 - 1997 (CDC, 2000)

Source: ATSDR (1999)

* includes PCBs 77, 81, 126 and 169)

Dioxin Exposure Variability

Dioxin intakes for general population may reach levels at least 3 times the mean

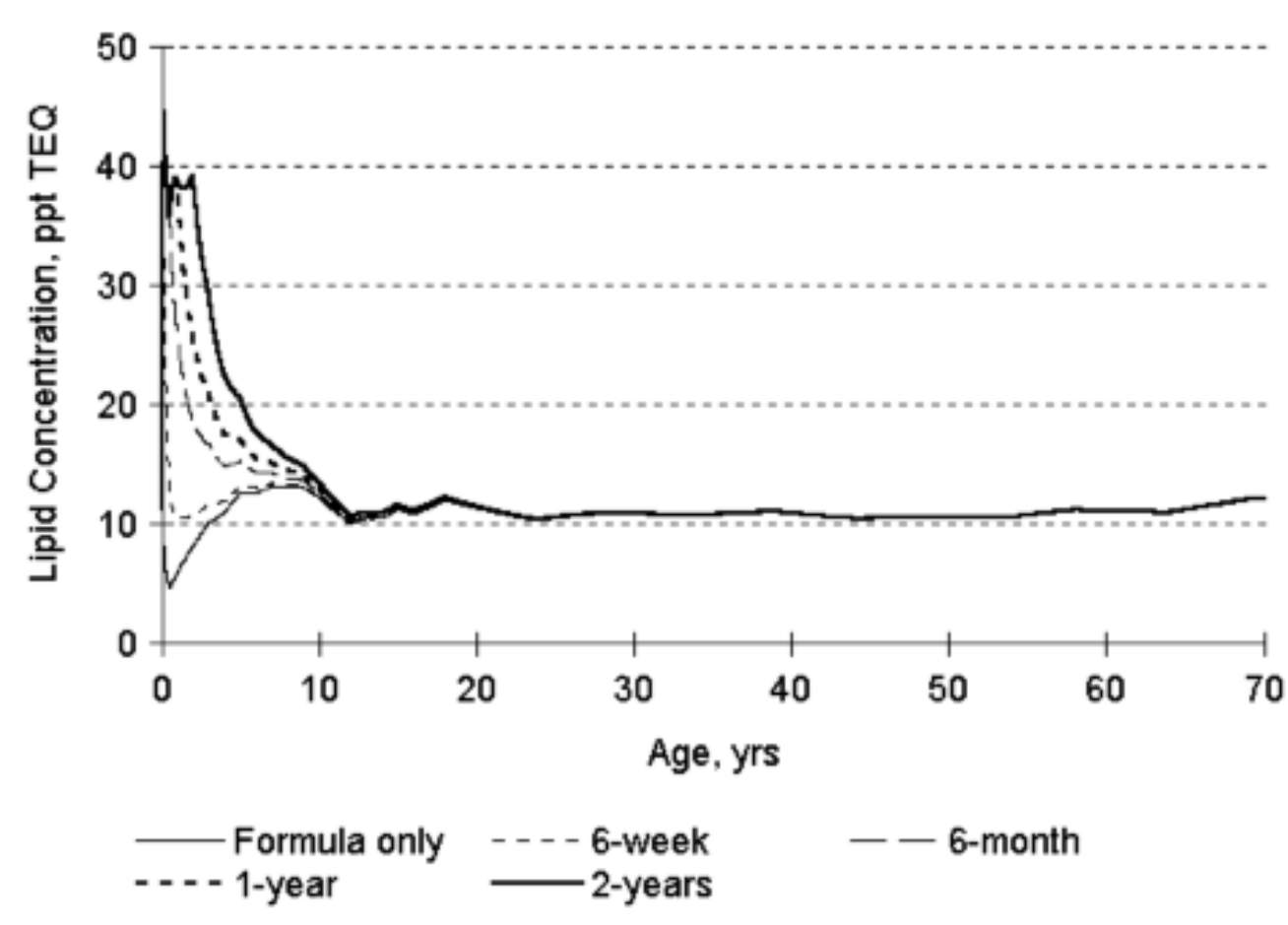
Support:

- ➔ *99th percentile total animal fat consumption is 3 times the mean*
- ➔ *99th percentile blood level is 3 times the mean*

Potentially highly exposed populations may exceed this range:

- ➔ *Nursing infants*
- ➔ *Subsistence fishers/farmers in contaminated areas*
- ➔ *Occupational groups (historical)*

Four Nursing Scenarios



Body Burden Concentrations in a Hypothetical Female Until Age 70
Under : formula only, 6-week, 6-month, 1 and 2 years nursing
Assumes current average body burden levels in breast milk and ~ 1 pg TEQ_{DFP}-WHO_{98} /kg-day thereafter

Dioxin Exposure Trends

➔ **Environmental levels:**

- *Peaked in late 60s/early 70s; declined since based on sediment data*
- *Decline also supported by Emissions Inventory which shows significant decrease from 1987 to 1995 (~80%)*

➔ **Human tissue data suggest current levels are about half of 1980 levels (55 to 25 pg TEQ_{DFP}/g lipid)**

➔ **Steady state PK modeling of current intake levels project tissue levels of about 11 pg TEQ_{DFP}/g lipid.**

U.S. Levels in Food
CDD/CDF/PCB TEQ_{WHO98} (whole weight basis)

Media	CDD/CDFs[a]	References	PCBs[a]	References	Total
Beef ppt	n=63 **0.18** ± 0.11 Range = 0.11 - 0.95	Winters et al. (1996a)	n = 63 **0.084**	Winters et al. (1996b)	**0.26**
Pork, ppt	n=78 **0.28** ± 0.28 Range = 0.15 - 1.8	Lorber et al. (1997b)	n = 78 **0.012**	Lorber et al. (1997b)	**0.29**
Poultry, ppt	n=78 **0.068** ± 0.070 Range = 0.03 - 0.43	Ferrario et al. (1997)	n = 78 **0.026**	Ferrario et al. (1997)	**0.094**
Milk, ppt	n=8 composites **0.018**	Lorber et al. (1998b)	n = 8 composites **0.0088**	Lorber et al. (1998b)	**0.027**
Dairy, ppt	n = 8 composites 0.12	Based on data from Lorber et al. (1998b)	n = 8 composites **0.058**	Based on data from Lorber et al. (1998b)	**0.18**
Eggs, ppt	n=15 composites **0.081**[e]	Hayward and Bolger (2000)	n = 18 plus 6 composites **0.10**[d,e]	Schecter et al. (1997) Mes and Weber (1989), Mes et al.	**0.13**
Vegetable Fats, ppt	n=30 **0.056** ± 0.24[g]	Versar (1996b)	n = 5 composites **0.037**[e]	Mes et al. (1991)	**0.09**
Freshwater Fish and Shellfish, ppt	n=222 **1.0**[d]	Fiedler et al. (1997), Jensen and Bolger (2000), Jensen et al. (2000), U.S. EPA (1992)	n = 1 composite of 10 samples plus 6 composites **1.2**[de]	Schecter et al. (1997) Mes and Weber (1989), Mes et al. (1991)	**2.2**
Marine Fish and Shellfish,	n=158 **0.26**[d]	Fiedler et al. (1997a), Jensen et al. (2000)	n = 1 composite of 13 **0.25**[d,e]	Schecter et al. (1997), Mes et al. (1991)	**0.57**

Sources and Pathways

Sources:

- Combustion
- Metal smelting, refining, processing
- Chemical manufacturing
- Biological and photochemical processes
- Reservoir sources

Pathways:

- Ingestion of soil, meats, dairy products, fish
- Inhalation of vapors and particulates
- Dermal contact with soils

Confidence Rating Scheme (Rating Quality of Data)

Category	Rating	Activity Level	Emission Factor
A	High	Comprehensive data	Comprehensive data
B	Medium	Based on limited data	Based on limited data
C	Low	Based on expert judgment	Derived from few tested facilities
D	Preliminary Estimate	Inadequate data	Inadequate for more than an order of magnitude estimate
E	Not quantifiable	Insufficient data	Insufficient data

Most Dioxin Releases Are to the Air